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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,904	12/02/2003	Kei Roger Aoki	16952CON1CIP3 (BOT)	4172

7590 03/29/2006

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EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/726,904	AOKI ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *6-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1 Applicant's claim for domestic priority under 35 U.S.C. 119(e), to Application No. 08/627,118 and 08/173,996 is acknowledged. The MPEP states that "however, if a claim in a continuation-in-part application recites a feature which was not disclosed or adequately supported by a proper disclosure under 35 U.S.C. 112 in the parent nonprovisional application, but which was first introduced or adequately supported in the continuation-in-part application such a claim is entitled only to the filing date of the continuation-in-part application." In the instant application, a method of treating blepharospasm using an effective amount of neurotoxic component of botulinum toxin free of a botulinum toxin complex protein was first introduced and adequately supported in the instant continuation-in-part application. The Parent application limited the disclosure of blepharospasm to a generic statement stating "[h]eretofore, Botulinum toxins, in particular Botulinum toxin type A, has been used in the treatment of a number of neuromuscular disorders and conditions involving muscular spasm; for example, strabismus, blepharospasm, pasmodic torticollis (cervical dystonia), oromandibular dystonia and spasmodic dysphonia (laryngeal dystonia). The parent application did not provide sufficient written description as to the effective amount to treat blepharospasm and thus priority to the parent application has been denied.

Election/Restrictions

2. Applicant's election of Group I, claims 1-5, in the reply filed on 2-6-06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. The request for cancellation of claims 6-28 is acknowledged. However, the claims have not been canceled since Applicants did not present a clean version of the claims indicating the canceled claims. Accordingly, the claims are still pending and are hereby withdrawn from consideration as drawn to non-elected groups.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balkan et al. or Han et al. in view of Tse et al. and Aoki et al. (US 6,113,915).

The claims are drawn to a method of treating strabismus using therapeutically effective amount of neurotoxin component of the botulinum toxin free of botulinum toxin protein.

Balkan et al. teaches the administration of botulinum toxin type A and type F for the treatment of strabismus (see abstract). The reference discloses that 37% of the patients treated with the toxin were cured and many showed significant improvement.

Han et al. describes the use of botulinum toxin type A in the treatment of strabismus (see abstract). The reference disclose a dosage of 1.24-5 units to a patient suffering from strabismus (abstract). Note that about 1.25-5 units ins inclusive of the claimed range of claim 6. Furthermore, the reference discloses the same dosage range, alleviation of strabismus would necessarily be achieved. The difference between the Han et al. or Balkan et al and the instant application is that the reference does not teach the use of botulinum toxin having a molecular weight of 150kda.

However, Tse et al. teach that purified neurotoxin with a molecular weight of 1.4kda and removing the Haemagglutinin complex by affinity chromatography (see page 494). The reference states that neurotoxin free of Haemagglutinin, when injected into the hind leg muscle of a rat, produced local paralysis within 24 hours (see page 494). Further, as with impure neurotoxin, pure neurotoxin (mw 140 kda) specifically and characteristically inhibited stimulated and spontaneous release of acetylcholine at the vertebrate neuromuscular junction (see page 499). It should be noted that it is well known in the art that botulinum toxin complexes inhibit the release of acetylcholine resulting in local paralysis of the muscle (see page 1-2 of the instant specification). Aoki et al. teaches that botulinum toxin complexes (MW greater than 150 kda) may result in slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection of botulinum toxin complex (see col. 5, lines 50-25). Therefore, it would have been obvious to one of ordinary skill it the art to use pure neurotoxin for the treatment of strabismus because pure neurotoxin has similar activity in the paralysis of muscles as complexed neurotoxin and has similar activity against spontaneous release of actetylcholine and because that botulinum toxin complexes (MW greater

than 150 kda) may result in slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection.

5. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balkan et al. or Han et al. in view of Aoki et al. (US 6,113,915) and Aoki et al. (20010018415).

The claims are drawn to a method of treating strabismus using therapeutically effective amount of neurotoxin component of the botulinum toxin free of botulinum toxin protein.

Balkan et al. teaches the administration of botulinum toxin type A and type F for the treatment of strabismus (see abstract). The reference discloses that 37% of the patients treated with the toxin were cured and many showed significant improvement.

Han et al. describes the use of botulinum toxin type A in the treatment of strabismus (see abstract). The reference disclose a dosage of 1.24-5 units to a patient suffering from strabismus (abstract). Note that about 1.25-5 units ins inclusive of the claimed range of claim 6. Furthermore, the reference discloses the same dosage range, alleviation of strabismus would necessarily be achieved. The difference between the Han et al. or Balkan et al and the instant application is that the reference does not teach the use of botulinum toxin having a molecular weight of 150kda.

Aoki et al. (US 6,113,915) teaches that botulinum toxin complexes (MW greater than 150 kda) may result in slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection of botulinum toxin complex (see col. 5, lines 50-25). Aoki et al. (US 20010018415) teach The neurotoxic component of Botulinum toxin has a molecular weight of about 150 kilodaltons and is thought to comprise a short polypeptide chain of about 50 kD which is considered to be responsible for the toxic properties of the toxin, i.e., by interfering with the exocytosis of acetylcholine, by decreasing the frequency of acetylcholine release, and a larger polypeptide chain of

about 100 kD which is believed to be necessary to enable the toxin to bind to the presynaptic membrane (see col. 1, paragraph 0007). Therefore, it would have been obvious to one of ordinary skill it the art to use pure neurotoxin for the treatment of strabismus because botulinum toxin complexes (MW greater than 150 kda) may result in slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection and the 150 kda portion of the toxin has a short polypeptide chain of about 50 kD which is considered to be responsible for the toxic properties of the toxin, i.e., by interfering with the exocytosis of acetylcholine, by decreasing the frequency of acetylcholine release, and a larger polypeptide chain of about 100 kD which is believed to be necessary to enable the toxin to bind to the presynaptic membrane.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-11 of copending Application No. 10/443,593.

Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The claims are drawn to a method of treating strabismus using therapeutically effective amount of neurotoxin component of the botulinum toxin free of botulinum toxin protein.

The copending application claims a method of treating strabismus by administering to a human patient a "therapeutically effective amount of neurotoxin component of the botulinum toxin free of botulinum toxin protein" (see claim 1). The application claims botulinum toxin types A, B, C, D, E F and G similar to the instant claims. Note that claim 9 of the US application claims the molecular weight of the toxin is 150 kilodaltons. The difference between the US application and the instant application is that the US application claims the method of treatment in humans, whereas the instant claims are drawn to any subject.

The MPEP states "[a] generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." Here, the US application of a specific subject falls within the generic genus of the instant application. Thus, the US application's claims and the instant claims are not patentably distinct from each other

This is a provisional obviousness-type double patenting rejection.

6. Claims 1-5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. US 6, 841, 156 in view of Tse et al. and Aoki et al.

The claims are drawn to a method of treating strabismus using therapeutically effective amount of neurotoxin component of the botulinum toxin free of botulinum toxin protein.

The US patent claims, method for treating a strabismus, the method comprising the step of administering to a human patient a therapeutically effective amount of botulinum toxin type B to treat strabismus, wherein the botulinum toxin type B is administered by intramuscular injection or by subcutaneous injection, and the administration of the botulinum toxin type B results in alleviation of the strabismus within 1 day to 7 days (see claim 1). The difference between the Han et al. or Balkan et al and the instant application is that the reference does not teach the use of botulinum toxin having a molecular weight of 150kda.

However, Tse et al. teach that purified neurotoxin with a molecular weight of 1.4kda and removing the Haemagglutinin complex by affinity chromatography (see page 494). The reference states that neurotoxin free of Haemagglutinin, when injected into the hind leg muscle of a rat, produced local paralysis within 24 hours (see page 494). Further, as with impure neurotoxin, pure neurotoxin (mw 140 kda) specifically and characteristically inhibited stimulated and spontaneous release of actetylcholine at the vertebrate neuromuscular junction (see page 499). It should be noted that it is well known in the art that botulinum toxin complexes inhibit the release of acetylcholne resulting in local paralysis of the muscle (see page 1-2 of the instant specification). Aoki et al. teaches that botulinum toxin complexes (MW greater than 150 kda) may result in slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection of botulinum toxin complex (see col. 5, lines 50-25). Therefore, it would have been obvious to one of ordinary skill it the art to use pure neurotoxin for the treatment of strabismus because pure neurotoxin has similar activity in the paralysis of muscles as complexed neurotoxin and has similar activity against spontaneous release of actetylcholine and because that botulinum toxin complexes (MW greater

than 150 kda) may result in slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection.

7. Claims 1-5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. US 6, 841, 156 in view of Aoki et al. (US 6,113,915) and Aoki et al. (20010018415).

The claims are drawn to a method of treating strabismus using therapeutically effective amount of neurotoxin component of the botulinum toxin free of botulinum toxin protein.

The US patent claims, method for treating a strabismus, the method comprising the step of administering to a human patient a therapeutically effective amount of botulinum toxin type B to treat strabismus, wherein the botulinum toxin type B is administered by intramuscular injection or by subcutaneous injection, and the administration of the botulinum toxin type B results in alleviation of the strabismus within 1 day to 7 days (see claim 1). The difference between the Han et al. or Balkan et al and the instant application is that the reference does not teach the use of botulinum toxin having a molecular weight of 150kda.

Aoki et al. (US 6,113,915) teaches that botulinum toxin complexes (MW greater than 150 kda) may result in slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection of botulinum toxin complex (see col. 5, lines 50-25). Aoki et al. (US 20010018415) teach The neurotoxic component of Botulinum toxin has a molecular weight of about 150 kilodaltons and is thought to comprise a short polypeptide chain of about 50 kD which is considered to be responsible for the toxic properties of the toxin, i.e., by interfering with the exocytosis of acetylcholine, by decreasing the frequency of acetylcholine release, and a larger polypeptide chain of about 100 kD which is believed to be necessary to enable the toxin to bind to the presynaptic

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can normally be reached on (571) 272-0974. The fax phone number of this group is (571)-273-8300.

2/20/06
ANISH GUPTA
PRIMARY EXAMINER